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Left atrial epithelioid hemangioendothelioma

Milan Lisy, MD,[a] Wolfram Beierlein, MD,[a] Hartmut Müller, MD, PhD,[b] Burkhard Bültmann, MD, PhD,[b] and Gerhard Ziemer, MD, PhD,[a] Tubingen, Germany

A case of cardiac epithelioid hemangioendothelioma is presented, occurring as a clinically silent pediculated left atrial tumor in a 61-year-old male patient who underwent pancreaticoduodenectomy for carcinoma of the pancreas 3 years previously. The tumor was completely resected with the presumptive clinical diagnosis of atrial myxoma. Histologic and immunohistochemical investigations demonstrated a mesenchymal tumor with antigen positivity for hemangioendotheliomas. Epithelioid hemangioendotheliomas are rare vascular tumors of the heart, histologically characterized by capillary-sized vessels lined by proliferating plump, often multilayered, epithelial-like endothelial cells with cytoplasmic vacuoles.[1] Similar to most other primary intracardiac tumors, epithelioid hemangioendotheliomas may be found incidentally or after causing congestive heart failure, pericardial effusions, outflow tract obstruction, or thromboembolic events. Because of the biologic behavior of epithelioid hemangioendotheliomas, they are regarded as fully malignant, rather than borderline neoplasms, and are to be resected radically to prevent metastatic embolic disease.

Primary cardiac tumors are rare and most commonly histologically benign, with only 30% of them exhibiting histologic signs of malignancy.[2] Clinically, they may be found incidentally by chest radiogram or by causing dysrhythmia, congestive heart failure, pericardial effusions, outflow tract obstruction, or thromboembolic events.[3]

The epithelioid hemangioendothelioma is histologically characterized by capillary-sized vessels lined by proliferating plump epithelial-like endothelial cells with cytoplasmic vacuoles, often multilayered. It is regarded as a malignant, rather than a borderline, neoplasm.

From the Department of Thoracic, Cardiac and Vascular Surgery,[a] and Department of Pathology,[b] Tübingen University Hospital, Tubingen, Germany.

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Address for reprints: Gerhard Ziemer, MD, PhD, Department of Thoracic, Cardiac and Vascular Surgery, Tübingen University Hospital, Hoppe-Seyler Straße 3, D-72076 Tübingen (E-mail: gdziemer@uni-tuebingen.de).

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Clinical Summary

A 61-year-old man presented with nonspecific abdominal pain 3 years after he underwent a pancreaticoduodenectomy (Whipple's procedure) for adenocarcinoma of the pancreas. He had arterial hypertension, noninsulin-dependent diabetes mellitus, and sleep-induced apnea syndrome. His medication included metoprolol, captopril, allopurinol, and pancreatic enzyme supplements. Specific tumor markers for the pancreas were normal (carcinoembryonic antigen 3 μg/L, cancer antigen 19-9 5 kU/L). His electrocardiogram showed sinus rhythm and first-degree atrioventricular block, without ST-T anomalies.

Computed tomography excluded intraabdominal masses and remote lymphatic metastases of his previous pancreatic carcinoma. The chest computed tomography scan showed a 3 $\times$ 3-cm noncalcified mass on the posterolateral wall of the left atrium, a rather atypical site for myxoma.

Transthoracic and transesophageal echocardiography demonstrated good left ventricle function without hypertrophy and a mobile pediculated left atrial mass displaying typical features of a myxoma. The mitral valve was not involved.

Angiocardiography showed neither valvular nor coronary abnormalities, demonstrating the vascular supply of the atrial tumor originating from the proximal circumflex coronary artery.

Elective surgery was performed through a midline sternotomy using hypothermic cardiopulmonary bypass (30°C) and cold antegrade blood cardioplegic cardiac arrest. The left atrial tumor was initially inspected through the right atrium and the persistent foramen ovale. As described preoperatively, the tumor was polypoid, pediculated, and, atypically for a myxoma, located on the left lateral atrial wall, far away from the interatrial septum. An approach through the left atrial appendage was deemed to be better suited for complete resection. After complete excision with an adjacent strip of myocardium, the proximal left lower pulmonary vein and its orifice had to be reconstructed with a patch of fresh autologous pericardium. The patent foramen ovale was closed with a direct suture.

The patient had an uneventful postoperative course and was discharged on postoperative day 8.

The tumor was 4.2 cm in diameter and consisted exclusively of epithelioid tumor cells in a myxoid matrix (Figure 1). The lesion was encapsulated in a fibrotic sheath. The tumor was resected in sano (R0). Immunohistochemically the tumor cells were negative for myxoma markers: CK 5/6, PAN-CK, actin, CD34, CD68,

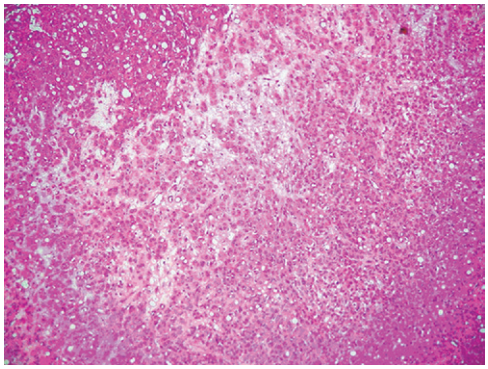

Figure 1. Epithelioid hemangioendothelioma is composed of solid sheets, cords, and chains of epithelioid endothelial cells. Several tumor cells form characteristic intracytoplasmatic vacuoles.

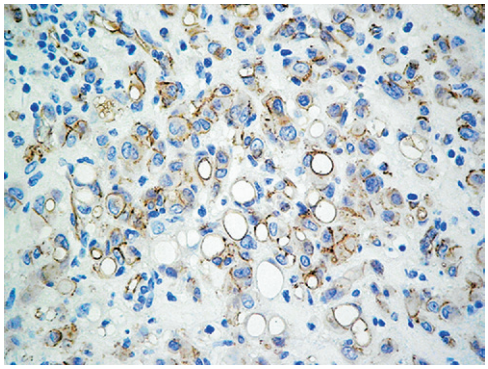

Figure 2. Positive CD31 membrane immunostaining in cohesive nests, short strands, and cells that form intracellular lumen.

protein S100, K-retinin, and desmin. The tumor stained positively for the hemangioendothelioma markers vimentin, CD31 (Figure 2), and BMA120. Immunostaining and electron microscopy confirmed the epithelioid hemangioendothelioma.

Nine months postoperatively, transthoracic echocardiography demonstrated good left ventricle function, no residual or recurrent tumor, no interatrial communication, and normal valves. Magnetic resonance imaging results were also normal.

Discussion

The most common primary tumor of the heart is the myxoma, representing 80% of surgically resected cardiac masses. Cardiac hemangiomas are rare. Clinically, they may be found incidentally or by causing the aforementioned symptoms. Sporadically, they are associated with gastrointestinal tract and cutaneous hemangiomas. If they are large, they may cause consumptive coagulopathy (Kasabach–Merritt syndrome).[4]

The epithelioid variant of vascular tumors is extremely rare. The epithelioid hemangioma represents the benign end of the spectrum, whereas the epithelioid angiosarcoma represents its malignant counterpart. The intermediate variant of this family, currently defined as epithelioid hemangioendothelioma, was initially considered as a low-grade malignant vascular tumor, but the occurrence of systemic metastases in 21%, which led to the death of 4 of 20 reported patients, led to the conclusion that epithelioid hemangioendothelioma is regarded as a malignancy.

Epithelioid hemangioendotheliomas have the aforementioned histologic characteristics, are usually positive for CD 31, CD34, factor VIII, and UEA-1 (Antigen Ulex Europaeus), and mostly negative for cytokeratin. Sarcomas and carcinomas, however, show the opposite immunohistochemical profile.[5]

There are no reports on the association of epithelioid hemangioendothelioma with tumors of other origins.

The epithelioid hemangioendothelioma is a rare, malignant (rather than borderline) vascular tumor of the heart that can potentially produce systemic metastases. Hemangioendotheliomas have to be dealt with in case of atypically localized atrial "myxoma." Cardiac epithelioid hemangioendotheliomas have to be resected to prevent metastatic embolism.

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